- (b) a region P3 comprising a double-stranded portion bound covalently at a bottom end to the remainder of the ribozyme and capped at a top end by a loop L3;
- (c) a region P2 comprising a double-stranded portion bound covalently at a bottom end to the remainder of the ribozyme;
- (d) a region P4 comprising a double-stranded portion bound covalently at a bottom end to the remainder of the ribozyme, wherein the first base-pair at the bottom end of P4 is a homopurine base-pair;
- (e) a double-stranded region P1.1 formed by base-pairing two nucleotides located between the substrate binding portion and the P4 region, with two nucleotides in the L3 loop; and
 - (f) a single-stranded region, J4/2, covalently bound at one end to the bottom end of P2 and covalently bound at the other end to the bottom end of P4.

11. (once amended) The nucleic acid enzyme according to claim 1, wherein the double-stranded portion of the P4 region comprises a sequence selected from the group consisting of 5'-GCAUGG-3', 5'-GCAUCG-3', 5'-GCAUGGG-3', 5'-GCAUGGG-3', 5'-GCAUGGG-3'.

- 14. (once amended) The nucleic acid enzyme of claim 1, wherein the substrate binding portion of the enzyme additionally comprises a seventh nucleotide attached to the 5'-most end of the six nucleotide sequence.
- 15. (once amended) The nucleic acid enzyme of claim 14, wherein the nucleotide other than a cytosine nucleotide is a nucleotide selected from the group consisting of an adenine nucleotide and a guanine nucleotide.
- 16. (once amended) The nucleic acid enzyme of claim 1, wherein the enzyme is composed of ribonucleotides.

Contich Contich

Ba



- 17. (once amended) The nucleic acid enzyme of claim 1, wherein the enzyme is composed of a mixture of ribonucleotides and deoxyribonucleotides.
- 18. (once amended) A method for cleaving a nucleic acid substrate with a nucleic acid enzyme at a cleavage site comprising mixing the nucleic acid enzyme according to any one of claims 1 to 17 with the substrate, wherein

the substrate includes a 7 nucleotide sequence with at least 6 nucleotides 3' to the cleavage site and at least 1 nucleotide 5' to the cleavage site, wherein the first nucleotide 3' to the cleavage site is a guanine nucleotide, the fourth nucleotide 3' to the cleavage site is a nucleotide other than a guanine nucleotide, and the nucleotide 5' to the cleavage site is a nucleotide other than a guanine nucleotide or a thymine nucleotide;

wherein

- (i) the first nucleotide 3' to the cleavage site is capable of forming a wobble pair with the enzyme,
- (ii) the second, third, fifth, and sixth nucleotides 3' to the cleavage site are capable of forming conventional Watson-Crick base pairs with the enzyme,
- (iii) the fourth nucleotide 3' to the cleavage site is capable of forming a triplet with the enzyme comprising a non-conventional Watson-Crick base pair and a conventional Watson-Crick base pair, and
- (iv) the ribonucleotide directly 5' to the cleavage site does not form a base pair with the enzyme.

REMARKS

Claims 1 to 19 are pending. Applicant has amended claims 1, 11 and 14 to 18. An Appendix including a marked-up copy of the amendments is attached, showing the changes. The attachment is captioned "Version with markings to show changes made."

23 contid